AMENDMENTS TO THE CLAIMS

1. (Original) A method of identifying an agent which modulates 2-oxoglutarate dependent oxygenase activity, the method comprising:

- contacting a 2-oxoglutarate dependent oxygenase and a test agent in the presence of a substrate comprising one or more ankyrin repeat, or fragment thereof, in conditions under which the substrate is hydroxylated in the absence of the test agent; and
- determining hydroxylation of the substrate

thereby determining whether or not the agent modulates 2-oxoglutarate dependent oxygenase activity.

2. (Original) A method according to claim 1, wherein the substrate is hydroxylated at an asparagine residue.

3. (Original) A method according to claim 2, wherein the asparagine residue is part of a valine-asparagine, aspartate-valine-asparagine, isoleucine-asparagine or leucine-asparagine sequence.

4. (Currently amended) A method according to claim 1 ~~any one of the preceding claims~~, wherein the substrate is IκB-α, p105, FEM-1, p19-INK-4d, GABPbeta, Tankyrase 1/2, 2-5A-d-R, Gankyrin, Myotrophin, M110, FGIF (Factor Inducing Foetal Globin), or a fragment of any thereof.

5. (Original) A method according to claim 4, wherein the substrate is p105 or a fragment thereof comprising Asn 778 of p105 or a peptide analogue of p105 or fragment thereof comprising an asparagine equivalent to Asn 778 of p105 and wherein hydroxylation of Asn 778 or of a said equivalent asparagine is determined.

6. (Currently amended) A method according to claim 1 ~~any one of the preceding claims~~, wherein the 2-oxoglutarate dependent oxygenase is a JmjC protein.

7. (Original) A method according to claim 6, wherein the JmjC protein is factor inhibiting hypoxia-inducible factor (FIH).

8. (Currently amended) A method according to claim 1 ~~any one of the preceding claims~~, wherein the hydroxylation of the substrate is determined by monitoring 2-oxoglutarate turnover.

9. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 7~~, wherein the hydroxylation of the substrate is determined by mass spectrometry.

10. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 7~~, wherein the hydroxylation of the substrate is determined by monitoring for transcription or expression of a reporter gene driven by a promoter regulated by an ankyrin repeat protein.

11. (Currently amended) A method according to claim 1 ~~any one of the preceding claims~~ further comprising formulating an agent identified as a modulator of 2-oxoglutarate dependent oxygenase activity with a pharmaceutically acceptable recipient.

12. (Original) A method of identifying an agent which selectively modulates activity of a first 2-oxoglutarate dependent oxygenase, the method comprising:

(a)(i) contacting a first 2-oxoglutarate dependent oxygenase and a test agent in the presence of a substrate comprising one or more ankyrin repeat, or fragment thereof, in conditions under which the substrate is hydroxylated in the absence of the test agent; and

(ii) determining hydroxylation of the substrate;

(b)(i) contacting a second 2-oxoglutarate dependent oxygenase and a test agent in the presence of a substrate comprising one or more ankyrin repeat, or fragment thereof, in conditions under which the substrate is hydroxylated in the absence of the test agent; and

(ii) determining hydroxylation of the substrate;

thereby determining whether or not the agent modulates activity of the first 2-oxoglutarate dependent oxygenase.

13. (Original) A method according to claim 12, wherein the test agent inhibits activity of the first 2-oxoglutarate dependent oxygenase.

14. (Currently amended) A method according to claim 12 ~~or 13~~, wherein the first 2-oxoglutarate dependent oxygenase is FIH.

15. (Currently amended) A method according to claim 12 ~~any one of claims 12 to 14~~, wherein the second 2-oxoglutarate dependent oxygenase is a PHD.

16. (Currently amended) A method according to claim 12 ~~or 13~~, wherein the first 2-oxoglutarate dependent oxygenase is a PHD.

17. (Currently amended) A method according to claim 16 ~~any one of claims 12, 13 and 16~~, wherein the second 2-oxoglutarate dependent oxygenase is FIH.

18. (Currently amended) A method according to claim 12 ~~any one of claims 12 to 17~~, wherein the substrate is hydroxylated at an asparagine residue ~~as defined in any one of claims 2 to 5~~.

19. (Original) A method of identifying an agent which selectively modulates 2-oxoglutarate dependent oxygenase activity on a first substrate, the method comprising:

(a)(i) contacting a 2-oxoglutarate dependent oxygenase and a test agent in the presence of a first substrate, or fragment thereof, in conditions under which the substrate is hydroxylated in the absence of the test agent; and

(ii) determining hydroxylation of the first substrate; and

(b)(i) contacting a 2-oxoglutarate dependent oxygenase and a test agent in the presence of a second substrate, or fragment thereof, in conditions under which the substrate is hydroxylated in the absence of the test agent; and

(ii) determining hydroxylation of the second substrate;

wherein at least one of said first and second substrates comprises one or more ankyrin repeat;

thereby determining whether or not the agent selectively modulates 2-oxoglutarate dependent oxygenase activity on a first substrate.

20. (Currently amended) A method according to claim 19, wherein the first and/or second substrate comprising one or more ankyrin repeat is hydroxylated at an asparagine residue ~~as defined in any one of claims 2 to 5~~.

21. (Currently amended) A method according to claim 19 ~~or 20~~, wherein the first substrate is HIF and the second substrate comprises one or more ankyrin repeat.

22. (Currently amended) A method according to claim 19 ~~or 20~~, wherein the second substrate is HIF and the first substrate comprises one or more ankyrin repeat.

23. (Currently amended) A method according to claim 19 ~~or 20~~, wherein the first and second substrates are different and each comprises one or more ankyrin repeat.

24. (Currently amended) A method according to claim 19 ~~any one of claims 19 to 23~~, wherein the 2-oxoglutarate oxygenase is a Jmjc protein ~~as defined in claim 6 or 7~~.

25. (Currently amended) A method according to claim 1 ~~any one of claims 1 to 24~~, wherein the test agent is a polypeptide comprising an ankyrin repeat or an analogue thereof.

26. (Original) A method according to claim 25, wherein the analogue is an ankyrin repeat that lacks an asparagine residue capable of being hydroxylated by 2-oxoglutarate dependent oxygenase.

27. (Currently amended) An agent identified by an assay method according to claim 1 ~~any one of the preceding claims~~.

28-31. (Cancelled)

32. (Original) A method of treating a condition associated with increased or decreased levels or activity of an ankyrin repeat-containing protein or the treatment of a condition where it is desired to modulate activity of an ankyrin repeat-containing protein comprising administering a therapeutically effective amount of an agent according to claim 27 to an individual in need thereof.

33. (Original) A method of modulating ankyrin repeat-containing protein mediated activity in a cell comprising contacting the cell with a substance which inhibits the asparagine hydroxylase activity of a 2-oxoglutarate dependent oxygenase.

34-35. (Cancelled)

36. (Currently amended) A method according to claim 33 ~~35~~, wherein the 2-oxoglutarate oxygenase is a Jmjc protein ~~as defined in claim 6 or 7~~.

37. (Currently amended) A method according to claim 32 ~~35 or 36~~, wherein the ankyrin repeat-containing protein ~~polypeptide~~ is IκB-α, p105, FEM-1, p19-INK-4d, GABPbeta, Tankyrase 1/2, 2-5A-d-R, Gankyrin, Myotrophin, M110 or FGIF ~~(Factor Inducing Foetal Globin), or a fragment of any thereof~~.

38. (New) A method according to claim 32, wherein said condition is selected from the group consisting of ischemia, cancer, inflammatory disorders, immune disorders, anaemia and beta thalassemia.